

CLAIMS

We claim:

5

1. A chimeric fusion protein comprising a bacteriorhodopsin protein amino acid sequence in which at least a portion of the protein is replaced with the structurally analogous region of a G protein-coupled
10 receptor protein.

Sub B1

2. The protein of claim 1, wherein the protein comprises substantially all of the amino acid sequence of bacteriorhodopsin except the intracellular loop 3 domain,
15 wherein the intracellular loop 3 domain of bacteriorhodopsin is replaced by at least a portion of the intracellular loop 3 domain of a G protein-coupled receptor protein.

3. The chimeric protein of claim 2, wherein the
20 intracellular loop 3 domain region corresponding to amino acid residues 171-179 of SEQ ID NO:2 is replaced with at least a portion of the intracellular loop 3 domain of a G protein-coupled receptor protein.

25 4. The chimeric protein of claim 2, wherein the protein is able to alter the rate of GTP-GDP exchange on a G protein *in vitro*.

5. The chimeric protein of claim 4, wherein the rate
30 of GTP-GDP exchange is increased.

Sub B2

6. A polynucleotide sequence encoding the chimeric fusion protein of claim 1.

35 7. A genetic construct comprising the polynucleotide sequence of claim 6, the polynucleotide sequence operably connected to a promoter sequence.

8. An archaeobacterium comprising the genetic construct of claim 7, wherein the polynucleotide sequence of the construct is expressible in the archaeobacterium.

5 9. The archaeobacterium of claim 8, wherein the archaeobacterium is characterized by reduced expression of wild type bacteriorhodopsin.

10 10. The archaeobacterium of claim 8, wherein the genetic construct is integrated into the archaeobacterium chromosome.

See B3 11. A method of producing a bacteriorhodopsin/G protein-coupled receptor chimeric fusion protein comprising
15 the step culturing an archaeobacterium comprising a genetic construct having a polynucleotide sequence that encodes a chimeric fusion protein having bacteriorhodopsin protein amino acid sequence in which at least a portion of the protein is replaced with the structurally analogous region
20 of a G protein-coupled receptor protein, the polynucleotide sequence operably connected to a promoter sequence functional in the archaeobacterium, wherein the polynucleotide sequence of the construct is expressible in the archaeobacterium, under suitable conditions and for a
25 period of time sufficient to allow expression of the chimeric fusion protein.

12. The method of claim 11, further comprising the step of partially purifying the chimeric fusion protein.

30

35

13. A method of testing a molecule for its ability to interact with the intracellular loop 3 of a G protein-coupled receptor comprising the steps of:

- (a) reacting a chimeric fusion protein of comprising a
5 substantially all of the bacteriorhodopsin protein amino
acid sequence amino acid sequence except the intracellular
loop 3 domain, wherein the intracellular loop 3 domain of
bacteriorhodopsin is replaced by at least a portion of the
intracellular loop 3 domain of a G protein-coupled receptor
10 protein with a test molecule under suitable reaction
conditions for a period of time sufficient to allow
interaction between the molecule and the protein; and
(b) detecting presence or absence of interaction
between the protein and the test molecule in the reaction
15 mixture.

14. The method of claim 13, wherein the chimeric
fusion protein of step (a) is able to promote GTP-GDP
exchange on a G protein in vitro, and wherein the detecting
20 step (b) includes an *in vitro* GTP-GDP exchange assay.

Add B4